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(73) Proprietor : **Beecham Group p.l.c.**
SB House Great West Road
Brentford Middlesex TW8 9BD (GB)

(72) Inventor : **Bolt, Ian James**
c/o Beecham Pharmaceuticals, Clarendon Road
Worthing, Sussex BN14 8QH (GB)
Inventor : **Merrifield, David Roy**
c/o Beecham Pharmaceuticals, Clarendon Road
Worthing, Sussex BN14 8QH (GB)
Inventor : **Carter, Paul Laurence**
c/o Beecham Pharmaceuticals, Clarendon Road
Worthing, Sussex BN14 8QH (GB)

(74) Representative : **Lockwood, Barbara Ann et al**
SmithKline Beecham, Corporate Patents, Great Burgh, Yew Tree Bottom Road
Epsom, Surrey KT18 5XQ (GB)

EP 0 396 335 B1

Description

This invention relates to pharmaceutical compositions for oral administration of antibiotics and other medicaments with unpleasant taste characteristics, and particularly to compositions formulated as chewable tablets.

From the point of view of bioavailability, the preferred form of administration of sparingly soluble medicaments such as a β-lactam antibiotics is often an aqueous suspension. However, there are problems associated with this form of administration. For example, such preparations in multidose form may have a limited shelf life; and usual methods of dose measurement lack accuracy. The bitter taste of many such medicaments is also a drawback.

Solid dosage forms which are swallowed, such as tablets and capsules, provide accurate dosage and avoid taste problems; but since they have to disintegrate in the gastrointestinal tract and the medicament has then to dissolve before it can be absorbed, absorption tends to be slower than from a suspension, and may be less than complete. Also, some patients have difficulty swallowing tablets and capsules, and there is a practical limit to the size, and therefore the dose, that can be swallowed.

Single dose powders for reconstitution in sachet form, and dispersible tablets, offer the advantages of suspensions without the problems of instability, measurement inaccuracy, difficulty in swallowing, or size limitation. However, residues from the dispersed formulation may be another reason for incomplete doses being swallowed. This is a particular problem with dispersible tablets, since the component granules may disperse into particles which are too large to remain evenly suspended.

In general, chewable tablets are advantageous in that they combine the accuracy of dosage associated with tablets, with the optimum bioavailability of suspensions. They may also accommodate larger doses than swallow tablets or capsules. Their acceptability is, however, reduced for bitter tasting medicaments, such as antibiotics, especially at higher doses, for example 500 mg. and above.

The dispersion properties of dispersible tablets can be facilitated by the inclusion of an acid/base couple in which the base liberates carbon dioxide when the components of the couple are dissolved in water. Such an effervescent couple has also been included in tablets for swallowing, to aid their disintegration in the gastrointestinal tract. It is also known to provide effervescent formulations of medicaments in water-soluble form so as to provide clear solutions of the antibiotics.

It has now been found that the inclusion of an effervescent couple in chewable tablets of bitter-tasting medicaments has surprising advantages with respect to palatability, in addition to assisting the break-up of the tablets in the mouth when chewed or sucked. Such 'fizzy chewable' tablets are thus well-accepted by patients, especially small children, who would otherwise find the medicine difficult to take and who might therefore refuse treatment. This contribution to improved patient compliance is also important with other classes of patients, for example the elderly, and those with mental illness.

Accordingly in one aspect the present invention provides a chewable tablet comprising a chewable base, a medicament having a bitter taste or unpleasant mouth-feel and an effervescent couple, said ingredients of the tablet being substantially uniformly distributed within the tablet.

This chewable composition is especially suitable for improving the taste characteristics of a range of medicaments, particularly for improving the taste of bitter-tasting medicaments, but clearly also provides a pleasant mode of administering any medicament, particularly those with an unpleasant mouth-feel even in the absence of a bitter taste, for example antacids.

Typical bitter-tasting medicaments are β-lactam antibiotics including penicillins such as amoxycillin or ampicillin, optionally in admixture with a β-lactamase inhibitor especially when a high dose is needed. Other medicaments whose taste can be improved include antihistamine H_2-receptor antagonists typically anti-ulcer compounds such as cimetidine, non-steroidal anti-inflammatories such as nabumetone, and bile acid sequestrants.

The effervescent couple comprises a basic ingredient and an acidic ingredient, the basic ingredient liberating carbon dioxide when it and the acidic ingredient are contacted with saliva or added water.

The amount of the effervescent couple is selected at a level sufficient to counter the taste of the medicament without itself causing discomfort in the patient's mouth. Normally the amount of effervescent couple will be less than that conventionally used in water-dispersible or solubilizable tablets.

Preferred antibiotics are amoxycillin and ampicillin, preferably amoxycillin trihydrate. A preferred β-lactamase inhibitor is clavulanic acid, preferably as potassium clavulanate. Typically, the ratio of antibiotic to inhibitor is 4:1 or 2:1 by weight, but ratios of 12:1 to 1:1 may be used. The weight of antibiotic in a unit dose may range from 125mg to 1g, expressed in terms of the activity of the antibiotic. The weight of antibiotic in the composition calculated as the free acid, may range from 5% to 50% based on the weight of the tablet. The weight of the β-lactamase inhibitor in the composition, calculated as the acid, may range from 0.4% to 30% based on the weight of the tablet.

Other medicaments used in the tablet of the invention will also typically comprise 5 to 50% of the tablet weight.

The effervescent couple typically comprises citric acid or sodium hydrogen citrate and sodium bicarbonate, but other physiologically acceptable acid/alkaline or alkaline earth metal carbonate mixtures may be used, for example tartaric, adipic, fumaric or malic acids, and sodium, potassium or calcium (bi)carbonates or sodium glycine carbonate.

In general it has been found that preferred taste characteristics are exhibited when the relative proportions of the components of the effervescent couple on a chemical molecular equivalent basis are in the range of 4:3 to 1:3, more preferably about 2:3, expressed as the ratio of molecular equivalent of the acidic component to the basic component. In terms of a preferred combination of citric acid and sodium bicarbonate these values represent on a weight basis, a range from 1:1 to 0.3:1, preferably 0.5:1 expressed as the ratio of acidic to basic component.

However, in some formulations, the choice of flavouring agents may result in optimisation of taste characteristics when there is an excess of acidic component, for example, on a chemical molecular equivalent basis of from about 11:3 to 4:3 expressed as the ratio of acidic to basic component. For the combination of citric acid and sodium bicarbonate this represents 5:1 to 1:1 on a weight basis.

The weight of the acidic component may be in the range 0.5% to 20%, preferably 1.5% to 5%, of the weight of the tablet.

The weight of the basic component may be in the range 0.5% to 30%, preferably 1.5% to 10%, of the weight of the tablet.

In general, taste testing shows that acceptable taste characteristics are found with the effervescent couple representing 6.25% to 30% of the final tablet weight, with a preference for 10-15% in chewable antibiotics tablets but up to 20% for some other materials, such as nabumetone.

Preferred combinations comprise citric acid (or sodium hydrogen citrate) or malic acid with sodium carbonate in a weight ratio of 0.5:1 to 1:1.

The chewable base may be any of those conventionally employed in chewable tablets, for example mannitol, sorbitol, dextrose, fructose or lactose alone or combination. The tablets may also contain conventional lubricants such as magnesium stearate, sweetening agents such as sodium saccharin and aspartame, and flavouring and colouring agents.

In another aspect of this invention disintegrating agents are incorporated into the chewable tablet so as to give the patient the option of dispersing the tablet in a small amount of water prior to administration.

Suitable disintegrating agents are cellulose products such as microcrystalline cellulose, microfine cellulose or hydroxy propyl cellulose, and other materials such as cross-linked polyvinyl pyrrolidone (PVP) or sodium starch glycollate, used singly or in admixture. Hitherto in attempts to provide a dispersible tablet which can also be chewed containing conventional, especially cellulose - based disintegrants, the latter impart an unpleasant mouth-feel. However this is masked effectively when combined with an effervescent couple in the chewable tablets of this invention.

When using disintegrating agents to impart dispersibility to the chewable tablets, the amount of effervescent couple may be maintained at the levels indicated above relative to the weight of the final chewable, dispersible tablet. In view of the additional taste load, amounts of effervescent couple in the upper regions of the indicated ranges may be preferred.

The disintegrant is typically added at amounts of 5% to 30%, preferably from 15 to 20%, based on the final weight of the tablet.

The ingredients discussed above may be formed into tablets by conventional techniques, for example either by direct compression, or first slugging some of the ingredients, milling the slugs, blending with the remaining ingredients, and then compressing, as appropriate.

The chewable tablets are preferably packaged in sealed protective containers, such as screw cap bottles, plastic or metal tubes, aluminium foil sachets, aluminium-foil backed blister packs. It may be appropriate to incorporate a desiccant in the packaging. Alternatively, an edible desiccant may be incorporated in the composition as disclosed in EP-A-0 049 061 (Beecham).

Preferably the tablets are in unit-dose form. The amount of medicament in a unit-dose will depend on the condition to be treated and the assay of the medicament. The unit-dose will be repeated according to the usual regime for the medicament.

The invention is illustrated by the following Examples.

Example 1

250 mg Dose Fizzy Chewable Tablet (β-lactam antibiotic)

Ingredi nts	mg/ tablet	(% w/w)
Amoxycillin Trihydrate equivalent to Amoxycillin free acid	250.00	41.667
Magnesium stearate	6.75	1.125
Citric acid	12.50	2.083
Sodium bicarbonate	25.00	4.167
Sodium saccharin	2.50	0.417
Lemon dry flavour	27.50	4.583
Lime dry flavour	1.38	0.230
Sorbitol B.P.	90.00	15.000
Mannitol U.S.P.	q.s.to	100%
	600 mg	

Example 2

375 mg Dose Fizzy Chewable Tablet (β-lactam antibiotic + β-lactamase inhibitor

Ingredient	mg/ tablet	(% w/w)
Amoxycillin Trihydrate equivalent to Amoxycillin free acid	250.00	20.833
Potassium Clavulanate equivalent to clavulanic acid	125.00	10.417
Magnesium stearate	12.0	1.000
Citric acid	17.5	1.458
Sodium bicarbonate	35.0	2.917
Sodium saccharin	5.0	0.417
Lemon dry flavour	50.0	4.167
Lime dry flavour	2.5	0.208
Sorbitol B.P.	180.00	15.000
Silica gel dessicant	80.0	6.667
Mannitol U.S.P.	q.s to	100%
	1200 mg	

Manufacturing Procedure for Examples 1, 2 and 3

All ingredients were reduced to th desired particle siz by milling, then blended in a planetary mixer, to produce a compression mix. The compression mix was th n tabl tted on a rotary tabletting press, to the desired tablet w ight.

Example 3 A and 3B

500mg NSAID Fizzy Chewable Tablets

500mg NSAID Fizzy Chewable Tablets

Ingredients	A mg	B mg
Nabumetone	500.00	500.00
Sodium Bicarbonate	50.0	50.00
Citric Acid Anhydrous Ph. Eur.	25.00	25.00
Sorbitol B.P.	180.00	180.00
Magnesium Stearate Ph. Eur.	13.50	13.50
Lemon Dry Flavour	55.00	-
Peppermint Flavour	-	12.00
Vanilla Flavour	-	12.00
Saccharin Sodium B.P.	5.00	5.00
Mannitol USP	1200.00 to	1200.00

Example 4

β-Lactam Antibiotic/β-Lactamase Inhibitor Fizzy Chewable Dispersible Tablet

Example 4A

EXCIPIENTS	Mg Per Tablet	%
*Amoxycillin Trihydrate (fa)	250.0	20.83
*Potassium Clavulanate (fa)	62.5	5.21
*Magnesium Stearate	12.0	1.00
*Citric Acid	48.0	4.00
*Sodium Bicarbonate	62.4	5.20
*Silica Gel Dessicant	38.4	3.20
PVP Cross-Linked Dried	72.0	6.00
Aspartame	16.8	1.40
Lemon Flavour	28.8	2.40
Lime Flavour	4.8	0.40
Mannitol	to 1200.0	to 100.00

* = Slugging mixture

Exampl 4B

	EXCIPIENTS	Mg Per Tablet	%
*	Amoxycillin Trihydrate (fa)	250.0	20.83
*	Potassium Clavulanate (fa)	62.5	5.21
*	Magnesium Stearate	12.0	1.00
*	Citric Acid Anhydrous	48.0	4.00
*	Sodium Bicarbonate	62.4	5.20
*	Silica Gel Dessicant	38.4	3.20
	PVP Cross-Linked Dried	72.0	6.00
	Aspartame	16.8	1.40
	Orange Flavour	25.0	2.08
	Pineapple Flavour	10.0	0.83
	Mannitol	to 1200.0	to 100.00

* Slugging Mixture

Example 4C

EXCIPIENTS	Mg Per Tablet	%
*Amoxycillin Trihydrate (fa)	250.0	20.83
*Potassium Clavulanate (fa)	62.5	5.21
*Magnesium Stearate	12.0	1.00
*Citric Acid	48.0	4.00
*Sodium Bicarbonate	62.4	5.20
*Silica Gel Dessicant	38.4	3.20
PVP Cross-Linked Dried	72.0	6.00
Microcrystalline cellulose	150.0	12.50
Aspartame	16.8	1.40
Lemon Flavour	28.8	2.40
Lime Flavour	4.8	0.40
Mannitol	to 1200.0	to 100.00

* = Slugging mixture

Exampl 4D

	EXCIPIENTS	Mg Per Tablet	%
*	Amoxycillin Trihydrate (fa)	250.0	20.83
*	Potassium Clavulanate (fa)	62.5	5.21
*	Magnesium Stearate	12.0	1.00
*	Citric Acid Anhydrous	48.0	4.00
*	Sodium Bicarbonate	62.4	5.20
*	Silica Gel Dessicant	38.4	3.20
	PVP Cross-Linked Dried	72.0	6.00
	Microcrystalline cellulose	150.0	12.50
	Aspartame	16.8	1.40
	Orange Flavour	25.0	2.08
	Pineapple Flavour	10.0	0.83
	Mannitol	to 1200.0	to 100.00

* Slugging Mixture

Manufacturing Procedure for Examples 4A/B/C/D

The materials marked * were slugged on a tabletting machine. The 'slugs' thus obtained were broken down by milling and then blended with the remaining ingredients to produce a compression mix. This mix was tabletted on a rotary tabletting machine to the desired tablet weight.

Claims

Claims for the following Contracting States : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE

1. A chewable tablet comprising a chewable base, a medicament having a bitter taste or unpleasant mouthfeel and an effervescent couple said ingredients of the tablet being substantially uniformly distributed within the tablet.

2. A tablet according to claim 1, in which the effervescent couple comprises 6.25 to 30% of the tablet weight.

3. A tablet according to claim 2 in which the effervescent couple comprises 10 to 20% of the tablet weight.

4. A tablet according to any one of claims 1 to 3 in which the chewable base is one or more of mannitol, sorbitol, dextrose, fructose or lactos .

5. A tablet according to any ne of claims 1 to 4 in which the ratio of the acidic component of the effervescent couple to the basic component is from 4:3 to 1:3 on a molecular equivalent basis.

6. A tablet according to any one of claims 1 to 4 in which the ratio of the acidic component of the effervescent couple to the basic component is from 11.5:3 to 4:3 on a molecular equivalent basis.

7. A tablet according to any one of claims 1 to 6 in which the effervescent couple comprises an acid component selected from citric acid, tartaric acid, adipic acid, fumaric acid and malic acid, or acid salts thereof.

8. A tablet according to any one of claims 1 to 7 in which the effervescent couple comprises an alkaline component selected from sodium, potassium or calcium (bi)carbonates or sodium glycine carbonate.

9. A tablet according to any one of claims 1 to 8 in which the effervescent couple comprises citric acid, sodium hydrogen citrate or malic acid with sodium bicarbonate in a weight ratio (acid:base) of 0.5:1 to 1:1.

10. A tablet according to any one of claims 1 to 9 further comprising one or more disintegrants.

11. A tablet according to claim 10 in which the disintegrant component is from 5 to 30% of the tablet weight.

12. A tablet according to claim 11 in which the disintegrant component is from 15 to 20% of the tablet weight.

13. A tablet according to claims 10, 11 or 12 in which the disintegrant is a cellulose-based product or a polvinyl pyrrolidone-based product or a starch-glycollate product.

14. A tablet according to any one of claims 1 to 13, in which the medicament is selected from antibiotics, anti-ulcer drugs, anti-inflammatory drugs, bile acid sequestrants and antacids.

15. A process for preparation of a tablet according to any preceding claim which comprises mixing a medicament with a chewable base and an effervescent couple and optionally a disintegrant, and forming a tablet from the mixture.

16. The use of a tablet according to any preceding claim comprising a medicament, a chewable base and an effervescent couple, and optionally a disintegrant, for oral administration of the medicament.

Claims for the following Contracting States : ES, GR

1. A process for preparation of a chewable tablet which comprises mixing a medicament having a bitter taste or unpleasant mouthfeel with a chewable base and an effervescent couple and forming a tablet from the mixture said ingredients of the tablet being substantially uniformly distributed with the tablet.

2. A process according to claim 1, in which the effervescent couple comprises 6.25 to 30% of the tablet weight.

3. A process according to claim 2 in which the effervescent couple comprises 10 to 20% of the tablet weight.

4. A process according to any one of claims 1 to 3 in which the chewable base is one or more of mannitol, sorbitol, dextrose, fructose or lactose.

5. A process according to any one of claims 1 to 4 in which the effervescent couple comprises an acid component selected from citric acid, tartaric acid, adipic acid, fumaric acid and malic acid, or acid salts thereof.

6. A process according to any one of claims 1 to 5 in which the effervescent couple comprises an alkaline component selected from sodium, potassium or calcium (bi)carbonates or sodium glycine carbonate.

7. A process according to any one of claims 1 to 6 in which the ratio of the acidic component of the effervescent couple to the basic component is from 4:3 to 1:3, on a molecular equivalent basis.

8. A process according to any one of claims 1 to 6 in which the effervescent couple comprises citric acid, sodium hydrogen citrate or malic acid with sodium bicarbonate in a weight ratio (acid:base) of 0.5:1 to 1:1.

9. A process according to any one of claims 1 to 8 further comprising one or more disintegrants.

10. A process according to claim 9 in which the disintegrant forms from 5 to 30% of the final tablet weight.

11. A process according to claim 9 or 10 in which th disintegrant is a cellulose-based product r a polvinyl pyrrolidone-based product or a starch glycollate product.

12. A process according to any on of claims 1 to 11, in which the medicament is selected from antibiotics, anti-ulcer drugs, anti-inflammatory drugs, bil acid sequestrants and antacids.

13. The use of a tablet prepared by any preceding claim, comprising a medicament, a chewable base and an effervescent couple, and optionally a disintegrant, for oral administration of the medicament.

Patentansprüche

Patentansprüche für folgende Vertragsstaaten : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE

1. Kautablette, umfassend eine kaubare Basis, ein Arzneimittel mit bitterem Geschmack oder unangenehmem Gefühl im Mund und eine Brausemischung, wobei die Bestandteile der Tablette im wesentlichen gleichförmig in der Tablette verteilt sind.

2. Tablette nach Anspruch 1, in der die Brausemischung 6.25 bis 30 % des Gewichts der Tablette umfaßt.

3. Tablette nach Anspruch 2, in der die Brausemischung 10 bis 20 % des Gewichts der Tablette umfaßt.

4. Tablette nach einem der Ansprüche 1 bis 3, in der die kaubare Basis aus Mannit, Sorbit, Dextrose, Fructose oder Lactose oder mehreren davon besteht.

5. Tablette nach einem der Ansprüche 1 bis 4, in der das Verhältnis des sauren Bestandteils der Brausemischung zum basischen Bestandteil 4:3 bis 1:3, bezogen auf Moläquivalente, beträgt.

6. Tablette nach einem der Ansprüche 1 bis 4, in dem das Verhältnis des sauren Bestandteils der Brausemischung zum basischen Bestandteil 11,5:3 bis 4:3, bezogen auf Moläquivalente, beträgt.

7. Tablette nach einem der Ansprüche 1 bis 6, in der die Brausemischung einen sauren Bestandteil, gewählt aus Zitronensäure, Weinsäure, Adipinsäure, Fumarsäure und Äpfelsäure oder Säuresalze davon, umfaßt.

8. Tablette nach einem der Ansprüche 1 bis 7, in der die Brausemischung einen alkalischen Bestandteil, gewählt aus Natrium-, Kalium- oder Calcium(hydrogen)carbonaten oder Natriumglycincarbonat, umfaßt.

9. Tablette nach einem der Ansprüche 1 bis 8, in der die Brausemischung Zitronensäure, Natriumhydrogencitrat oder Äpfelsäure mit Natriumhydrogencarbonat in einem Gewichtsverhältnis (Säure:Base) von 0,5:1 bis 1:1 umfaßt.

10. Tablette nach einem der Ansprüche 1 bis 9, die weiter ein oder mehrere Sprengmittel umfaßt.

11. Tablette nach Anspruch 10, in der das Sprengmittel 5 bis 30 % des Gewichts der Tablette beträgt.

12. Tablette nach Anspruch 11, in der das Sprengmittel 15 bis 20 % des Gewichts der Tablette beträgt.

13. Tablette nach den Ansprüchen 10, 11 oder 12, in der das Sprengmittel ein Produkt auf Cellulosebasis oder ein Produkt auf Polyvinylpyrrolidon-Basis oder ein Stärke-Glycollat-Produkt ist.

14. Tablette nach einem der Ansprüche 1 bis 13, in der das Arzneimittel gewählt aus Antibiotika, Arzneimittel gegen Geschwüre, entzündungshemmende Arzneimittel, Gallensäuresequester und Antacida ist.

15. Verfahren zur Herstellung einer Tablette nach einem der vorstehenden Ansprüche, umfassend das Mischen eines Arzneimittels mit einer kaubaren Basis und einer Brausemischung und gegebenenfalls einem Sprengmittel und Formen einer Tablette aus dem Gemisch.

16. Verwendung einer Tablette nach einem der v rstehenden Ansprüche, umfass nd ein Arzneimittel, ein kaubare Basis und ine Brausemischung und g g ben nfalls ein Sprengmittel, für orale Verabreichung des Arzn lmitt ls.

Patentansprüche für folgende Vertragstaaten: ES, GR

1. Verfahren zur Herstellung einer Kautablette, umfassend das Mischen eines Arzneimittels mit bitterem Geschmack oder unangenehmem Gefühl im Mund mit einer kaubaren Basis und einer Brausemischung und Bilden einer Tablette aus dem Gemisch, wobei die Bestandteile der Tablette im wesentlichen gleichförmig in der Tablette verteilt sind.

2. Verfahren nach Anspruch 1, wobei die Brausemischung 6.25 bis 30 % des Gewichts der Tablette umfaßt.

3. Verfahren nach Anspruch 2, wobei die Brausemischung 10 bis 20 % des Gewichts der Tablette umfaßt.

4. Verfahren nach einem der Ansprüche 1 bis 3, wobei die kaubare Basis aus Mannit, Sorbit, Dextrose, Fructose oder Lactose oder mehreren davon besteht.

5. Verfahren nach einem der Ansprüche 1 bis 4, wobei die Brausemischung einen sauren Bestandteil, gewählt aus Zitronensäure, Weinsäure, Adipinsäure, Fumarsäure und Äpfelsäure oder Säuresalze davon, umfaßt.

6. Verfahren nach einem der Ansprüche 1 bis 5, wobei die Brausemischung einen alkalischen Bestandteil, gewählt aus Natrium-, Kalium- oder Calcium(hydrogen)carbonaten oder Natriumglycincarbonat, umfaßt.

7. Verfahren nach einem der Ansprüche 1 bis 6, wobei das Verhältnis des sauren Bestandteils der Brausemischung zum basischen Bestandteil 4:3 bis 1:3, bezogen auf Moläquivalente, beträgt.

8. Verfahren nach einem der Ansprüche 1 bis 6, wobei die Brausemischung Zitronensäure, Natriumhydrogencitrat oder Äpfelsäure mit Natriumhydrogencarbonat in einem Gewichtsverhältnis (Säure:Base) von 0,5:1 bis 1:1 umfaßt.

9. Verfahren nach einem der Ansprüche 1 bis 8, das weiter ein oder mehrere Sprengmittel umfaßt.

10. Verfahren nach Anspruch 9, wobei das Sprengmittel 5 bis 30 % des endgültigen Gewichts der Tablette beträgt.

11. Verfahren nach Anspruch 9 oder 10, wobei das Sprengmittel ein Produkt auf Cellulosebasis oder ein Produkt auf Polyvinylpyrrolidon-Basis oder ein Stärke-Glycollat- Produkt ist.

12. Verfahren nach einem der Ansprüche 1 bis 11, in dem das Arzneimittel gewählt aus Antibiotika, Arzneimittel gegen Geschwüre, entzündungshemmende Arzneimittel, Gallensäuresequester und Antacida ist.

13. Verwendung einer nach einem der vorstehenden Ansprüche hergestellten Tablette, umfassend ein Arzneimittel, eine kaubare Basis und eine Brausemischung und gegebenenfalls ein Sprengmittel, für orale Verabreichung als Arzneimittel.

Revendications

Revendications pour les Etats contractants suivants : AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE

1. Tablette à mâcher comprenant une base de mâchage, un médicament ayant un goût amer ou donnant une sensation désagréable dans la bouche et un couple effervescent, ces composants de la tablette étant distribués de façon pratiquement uniforme dans la tablette.

2. Tablette suivant la revendication 1, dans laquelle le couple effervescent représente 6,25% à 30% du poids de la tablette.

3. Tablette suivant la revendication 2, dans laquelle le couple effervescent représente 10% à 20% du poids de la tablette.

4. Tablette suivant l'une des revendications 1 à 3, dans laquelle la base de mâchage est constituée par un

u plusi urs des composés comprenant l mannit l, l sorbitol, le dextrose, l fructose ou l lactose.

5. Tablette suivant l'une des revendications 1 à 4, dans laquelle le rapport du composant acid du couple effervescent au composant basique est d 4:3 à 1:3 sur une base équivalent moléculaire.

6. Tablette suivant l'une des revendications 1 à 4, dans laquelle le rapport du composant acide du couple effervescent au composant basique est de 11,5:3 à 4:3 sur une base équivalente moléculaire.

7. Tablette suivant l'une des revendications 1 à 6, dans laquelle le couple effervescent comprend un composant acide choisi parmi l'acide citrique, l'acide tartrique, l'acide adipique, l'acide furnarique et l'acide malique ou leurs sels d'acide.

8. Tablette suivant l'une des revendications 1 à 7, dans laquelle le couple effervescent comprend un composant alcalin choisi parmi les carbonates et carbonates acides de sodium, de potassium ou de calcium ou le carbonate de glycine et de sodium.

9. Tablette suivant l'une des revendications 1 à 8, dans laquelle le couple effervescent comprend de l'acide citrique, du citrate acide de sodium ou de l'acide malique avec du carbonate acide de soidum selon un rapport en poids (acide:base) de 0,5:1 à 1:1.

10. Tablette suivant l'une des revendications 1 à 9, comprenant de plus un ou plusieurs agents de désagrégation.

11. Tablette suivant la revendication 10, dans laquelle le composant de désagrégation représente de 5 à 30% du poids de la tablette.

12. Tablette suivant la revendication 11, dans laquelle le composant de désagrégation représente de 15 à 20% du poids de la tablette.

13. Tablette suivant l'une quelconque des revendications 10, 11 ou 12, dans laquelle l'agent de désagrégation est un produit à base de cellulose ou un produit à base de polyvinyl pyrrolidone ou un produit de type glycolate d'amidon.

14. Tablette suivant l'une quelconque des revendications 1 à 13 dans laquelle le médicament est choisi parmi des antibiotiques, des médicaments anti-ulcèreux, des médicaments anti-inflammatoires, des séquestrants d'acides biliaires et des anti-acides.

15. Procédé pour la préparation d'une tablette suivant l'une quelconque des revendications précédentes, qui comprend le mélange d'un médicament avec une base de mâchage et un couple effervescent et éventuellement un agent de désagrégation, et la mise du mélange sous forme de tablette.

16. Utilisation d'une tablette suivant l'une quelconque des revendications précédentes, comprenant un médicament, une base de mâchage et un couple effervescent et éventuellement un agent de désagrégation, pour l'administration par voie orale du médicament.

Revendications pour les Etats contractants suivants : ES, GR

1. Procédé pour la préparation d'une tablette à mâcher, qui comprend le mélange d'un médicament ayant un goût amer ou donnant une sensation désagréable dans la bouche, avec une base de mâchage et un couple effervescent, et la mise du mélange sous forme d'une tablette, ces composants de la tablette étant distribués de façon pratiquement uniforme dans la tablette.

2. Procédé suivant la revendication 1, dans lequel le couple effervescent représente 6,25% à 30% du poids de la tablette.

3. Procédé suivant la revendication 2, dans lequel le couple effervescent représente 10% à 20% du poids de la tablette.

4. Procédé suivant l'une des revendicati ns 1 à 3, dans lequel la bas d mâchage est constituée par un u plusi urs des composés comprenant le mannit l, le sorbit l, le d xtrose, le fructose ou le lactose.

5. Procédé suivant l'une des revendications 1 à 4, dans lequ l couple effervescent comprend un composant acide choisi parmi l'acide citrique, l'acide tartrique, l'acide adipique, l'acide fumarique et l'acide malique ou leurs sels d'acide.

6. Procédé suivant l'une des revendications 1 à 5, dans lequel l couple efferv scent comprend un composant alcalin choisi parmi les carbonates et carbonates acides de sodium, de potassium ou de calcium ou le carbonate de glycine et de sodium.

7. Procédé suivant l'une des revendications 1 à 6, dans lequel le rapport du composant acide du couple effervescent au composant basique est de 4:3 à 1:3 sur une base équivalente moléculaire.

8. Procédé suivant l'une des revendications 1 à 6, dans lequel le couple effervescent comprend de l'acide citrique, du citrate acide de sodium ou de l'acide malique avec du carbonate acide de soidum selon un rapport en poids (acide:base) de 0,5:1 à 1:1.

9. Procédé suivant l'une des revendications 1 à 8, comprenant de plus un ou plusieurs agents de désagrégation.

10. Procédé suivant la revendication 9, dans lequel l'agent de désagrégation représente de 5 à 30% du poids de la tablette finale.

11. Procédé suivant les revendications 9 ou 10, dans lequel l'agent de désagrégation est un produit à base de cellulose ou un produit à base de polyvinyl pyrrolidone ou un produit de type glycolate d'amidon.

12. Procédé suivant l'une quelconque des revendications 1 à 11, dans laquelle le médicament est choisi parmi des antibiotiques, des médicaments anti-ulcèreux, des médicaments anti-inflammatoires, des séquestrants d'acides biliaires et des anti-acides.

13. Utilisation d'une tablette suivant l'une quelconque des revendications précédentes, comprenant un médicament, une base de mâchage et un couple effervescent et éventuellement un agent de désagrégation, pour l'administration par voie orale du médicament.